UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/581,052	03/30/2007	Francis Vocanson	71247-0059	7108

22902 7590 05/14/2008

CLARK & BRODY
1090 VERMONT AVENUE, NW
SUITE 250
WASHINGTON, DC 20005

EXAMINER	
WHISENANT, ETHAN C	

ART UNIT	PAPER NUMBER
1634	

MAIL DATE	DELIVERY MODE
05/14/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/581,052	VOCANSON ET AL.	
	Examiner	Art Unit	
	Ethan Whisenant, Ph.D.	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 MAY 06*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 May 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

NON-FINAL ACTION

1. The applicant's Preliminary Amendment filed 30 MAY 06 has been entered. Following the entry of the Preliminary Amendment, **Claim(s) 1-22** is/are pending.

35 USC § 112- 2nd Paragraph

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

CLAIM REJECTIONS under 35 USC § 112- 2ND PARAGRAPH

3. **Claim(s) 1-22** is/are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 3, 6, and 18 are indefinite because of the use of the word "preferably" The use of exemplary claim language makes these claims indefinite. See the MPEP at 2173.05(d). It is well established that the description of examples or preferences is properly set forth in the specification rather than the claims. If stated in the claims, examples and preferences lead to confusion over the intended scope of a claim. Ex parte Hall, 83 USPQ 38 (Bd. App. 1949).

Claim 1 is also indefinite in that it is unclear as to what is intended by the phrase "on the one hand, and on the other hand"

Claim 5 is indefinite in view of the phrase "for example derivatives of luminol". The use of exemplary claim language makes this claim indefinite. See the MPEP at 2173.05(d). It is well established that the description of examples or

preferences is properly set forth in the specification rather than the claims. If stated in the claims, examples and preferences lead to confusion over the intended scope of a claim. Ex parte Hall, 83 USPQ 38 (Bd. App. 1949).

Claims 8 are indefinite because of the use of the phrase "in particular". The use of exemplary claim language makes these claims indefinite. See the MPEP at 2173.05(d). It is well established that the description of examples or preferences is properly set forth in the specification rather than the claims. If stated in the claims, examples and preferences lead to confusion over the intended scope of a claim. Ex parte Hall, 83 USPQ 38 (Bd. App. 1949).

Claim 9 is indefinite in view of the phrase "gold en outside" It is unclear what is intended.

Claim 10 is indefinite in view of the phrase "ZrO_2,LN_2O_3" It is unclear what is intended. It appears a space is required after the recitation of ZrO_2, such that the phrase should read "ZrO_2, LN_2O_3". Please correct.

Claim 18 is also indefinite in light of the phrase "at least one alcohol, amine, sulphonate, carboxylic acid or phosphate function". Perhaps, the applicant intended this phrase to read "at least one alcohol, amine, sulphonate, carboxylic acid or phosphate functional group (or functionality)". Please clarify.

Claim 19 indefinite because of the use of the phrase "in particular". The use of exemplary claim language makes this claim indefinite. See the MPEP at 2173.05(d). It is well established that the description of examples or preferences is properly set forth in the specification rather than the claims. If stated in the claims, examples and preferences lead to confusion over the intended scope of a claim. Ex parte Hall, 83 USPQ 38 (Bd. App. 1949).

Claim 19 is also indefinite in light of the non-sequitur phrase "or alcoholic" on line 6. Please clarify.

Claim 20 is indefinite because the phrases "the organic probe molecules the molecules having luminescent activity " lack proper antecedent basis.

Claim 22 is indefinite because of the use of the phrase "in particular" The use of exemplary claim language makes this claim indefinite. See the MPEP at 2173.05(d). It is well established that the description of examples or preferences is properly set forth in the specification rather than the claims. If stated in the claims, examples and preferences lead to confusion over the intended scope of a claim. Ex parte Hall, 83 USPQ 38 (Bd. App. 1949).

35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that may form the basis for rejections set forth in this Office action:

> A person shall be entitled to a patent unless --
>
> **(a)** the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> **(b)** the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> **(e)** the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
> or
> **(e)** the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

5. The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a)** A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligations under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

CLAIM REJECTIONS UNDER 35 USC § 102/103

8. **Claim(s) 1, 13-17** is/are rejected as obvious under 35 U.S.C. 103(a) over Buining et al. [WO99/01766 (1999)].

Buining et al. teach a hybrid probe particles comprising all of the limitations of Claim 1 except these authors do not explicitly teach grafting onto the surface of gold nanoparticles organic probe molecules via gold-sulphur bonds. However the examiner considers this limitation (i.e. the utilization of gold-sulphur bonds) to be inherent to Buining et al. in that these authors teach on page 22, lines 8-27:

> "Another advantage of these silane-stabilized gold particles is the easy ability to bind more than one molecule simultaneously to the mercaptosilane shell of each gold particle. For instance, besides protected sulfhydryl groups for the bioreagent coupling, also fluoresceins and/or biotin molecules can be attached to the same particle, rendering a multi-functional gold probe. The fluorochrome-labeled gold particles serve as easily detectable labels to check their conjugation to high molecular weight biomolecules, but they can also be used for immunocytochemical analysis. Immuno-chemical labeling prepared for electron microscopy can first easily be confirmed by fluorescence microscopy to obtain information at the cellular level before EM is applied for information at the sub-cellular level. Concerning the fluorescent signal, the siloxane cage has an insulating effect on the electronic interaction between the energy levels of the gold (quantum-) particle and those of the fluorescent molecules. This way, quenching of the fluorescence signal is reduced, a problem especially serious for non-covalently bound gold probes."

As regards the limitation "luminescent molecules" see at least for example the fluorescein taught on p.22. Furthermore, by the applicant's own admission the strength of gold-sulphur bonds were known making it clear that the bonding of organic molecules to gold surface via gold-sulphur bonds was known prior to the instant

invention. See for example paragraph [0046]. Finally note that the metes and bounds of what is intended by the phrase gold-sulphur bonds is ambiguous at best in light of the disclosure of the instant application. No where is the phrase gold-sulphur bonds defined. Therefore, the coupling of the bioreagent via the protected sulfhydryl groups reads on "gold-sulphur bonds". Finally, it is noted that Buining et al. is silent as regards the number of organic molecules/ luminescent molecules grafted to the surface of their gold particles. However, in view of the ambiguity of Claim 1 the examiner asserts that at a minimum Buining et al. reasonably suggest that at least one organic molecule and a limited number (i.e. at least about 10) of luminescent molecules be conjugated to the gold nanoparticles of Buining et al. Furthermore, absent an unexpected result with the number of organic molecules/luminescent molecules recited it would have been *prima facie* obvious to the ordinary artisan that essentially any number of organic molecules/luminescent molecules could be utilized with a reasonable expectation of success.

Claim 13 is drawn to an embodiment of the hybrid probe particles of Claim 1 wherein the nanoparticles of gold has a diameter in the range of 4-20 nm.

Buining et al. teach this limitation. See, for example, p.11, lines 1-6.

Claim 14 is drawn to an embodiment of the hybrid probe particles of Claim 1 wherein 1 to 10 organic molecules are grafted onto the nanoparticles of gold.

Buining et al. teach this limitation. Note that Buining et al. teach the grafting of at least one organic molecule (i.e. an antibody) onto the nanoparticle of gold. As the claim is a comprising type claim it is asserted that Buining et al. teach all of the limitations of Claim 14.

Claim 15 is drawn to an embodiment of the hybrid probe particles of Claim 1 wherein the organic probes are selected from a defined group which includes proteins of the antibody type and polynucleotides type DNA , RNA or oligonucleotides.

Buining et al. teach these limitations. See at least pp. 22 -23.

Claim 16 is drawn to an embodiment of the hybrid probe particles of Claim 14 wherein the organic probes are thiolated oligonucleotides or attached to a thiolated spacer.

Admittedly, Buining et al. is silent as to exactly how the oligos are attached to the gold nanoparticles they describe However, these authors do teach numerous different coupling strategies that can be use with their gold nanoparticles, in addition, end thiolated oligonucleotides were well known at the time of the invention (Official Notice) as was there attachment to solid surfaces via these thiolated ends. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to attach the oligonucleotide to the gold nanoparticles using a thiolated spacer.

Claim 17 is drawn to an embodiment of the hybrid probe particles of Claim 14 wherein the organic probes molecules are molecules allowing biotin-streptavidin interaction.

Buining et al. teach these limitations. See at least p. 22, lines 8-27

CLAIM REJECTIONS UNDER 35 USC § 103

9. **Claim(s) 5** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Buining et al. [WO99/01766 (1999)] in view of West et al. [US 6,530,944 (MAR 03)]

Claim 5 is drawn to an embodiment of the hybrid probe particles of Claim 1 wherein the molecules with luminescent activity are electrochemiluminescent or chemiluminescent compounds.

Buining et al. reasonably suggest a hybrid probe particles comprising all of the limitations of Claim 5 except these authors do not teach an embodiment wherein the molecules with luminescent activity are electrochemiluminescent or cheiluminescent

compounds. However, as evidenced by at least West et al. molecules with luminescent activity that are electrochemiluminescent or cheiluminescent compounds. See, for example, Column 13, lines 14-20, as was there use as reporters in biological assay. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the gold nanoparticles of Buining et al. wherein the molecules with luminescent activity that are electrochemiluminescent or cheiluminescent compounds of West et al. are used in place of the fluoresceins taught by Buining et al. Please note that substitution of one well known method/reagent with known properties for a second well known method/reagent with well known properties would have been *prima facie* obvious to the ordinary artisan at the time of the invention in the absence of an unexpected result. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

10. Claim(s) 7 is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Buining et al. [WO99/01766 (1999)] in view of Raymond et al. [US 6,515,113(2003)].

Claim 7 is drawn to an embodiment of the hybrid probe particles of Claim 1 wherein the molecules with luminescent activity are lanthanide complexes.

Buining et al. reasonably suggest the hybrid probe particles comprising all of the limitations of Claim 7 except these authors do not explicitly teach an embodiment wherein the molecules with luminescent activity are lanthanide complexes. However, as evidenced by at least Raymond et al. the use of luminescent lanthanide complexes as markers in biological assays was well known prior to the instant invention. See at least the abstract of Raymond et al. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the gold nanoparticles of Buining et al. wherein the luminescent

lanthanide complexes of Raymond et al. are used in place of the reporters taught by Buining et al. Please note that substitution of one well known method/reagent with known properties for a second well known method/reagent with well known properties would have been *prima facie* obvious to the ordinary artisan at the time of the invention in the absence of an unexpected result. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

11. Claim(s) 8 is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Buining et al. [WO99/01766 (1999)] in view of Riss [US 6,350,452(2002)].

Claim 8 is drawn to an embodiment of the hybrid probe particles of Claim 1 wherein the molecules with luminescent activity are derivatives of rhodamine.

Buining et al. reasonably suggest the hybrid probe particles comprising all of the limitations of Claim 8 except these authors do not explicitly teach an embodiment wherein the molecules with luminescent activity are derivatives of rhodamine. However, as evidenced by at least Riss the use of luminescent derivatives of rhodamine as markers in biological assays was well known prior to the instant invention. See at least, Column 4, lines 46-58. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the gold nanoparticles of Buining et al. wherein the luminescent derivatives of rhodamine of Riss are used in place of the reporters taught by Buining et al. Please note that substitution of one well known method/reagent with known properties for a second well known method/reagent with well known properties would have been *prima facie* obvious to the ordinary artisan at the time of the invention in the absence of an unexpected result. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when

combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

CONCLUSION

12. **Claim(s) 1-22** is/are rejected and/or objected to for the reason(s) set forth above.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ethan Whisenant, Ph.D. whose telephone number is (571) 272-0754. The examiner can normally be reached Monday-Friday from 8:30AM - 5:30PM EST or any time via voice mail. If repeated attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached at (571) 272-0735.

The Central Fax number for the USPTO is (571) 273-8300. Please note that the faxing of papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989).

/Ethan Whisenant/
Primary Examiner
Art Unit 1634

EXAMINER SEARCH NOTES

09 MAY 08 - ECW

Databases searched: USPATFULL, USPG-PUBS, JAPIO and EUROPATFULL via EAST &

CAplus, Medline and BIOSIS via STN

Reviewed the parent(s), if any, and any search(es) performed therein : see the BIB data sheet

Reviewed, the search(es), if any, performed by prior examiners

Search terms:

Inventor(s) : e.g. Thompson A?/au

gold with (particle$ or nonoparticle$)
(oligonucleotide$ or probe$ or ligand$ or antibody or antibodies)
molecules with (luminescent or fluorescent or fluoresce)
fluorophore$
thio or thiolated
gold-sulphur bond$
hydrogen tetrachloroaurate
citrate
tannic acid
$NaBH_4$